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The Effect of High Intensity Focused Ultrasound Combined with Ethanol on the Lesion of Porcine Liver in Vitro

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ABSTRACT

Introduction: As a non-invasive method of tumor hyperthermia, high intensity focused ultrasound (HIFU) has been widely used in the treatment of various solid tumors in recent years. The purpose of this study was to investigate the effect of HIFU combined with ethanol on biological tissue lesions.

Material and Methods: Firstly, 0.5ml 95% ethanol was injected into the porcine liver tissue in vitro, then HIFU was used to irradiate the porcine liver. The B-mode ultrasound and needle hydrophone were used to monitor the cavitation. A thermocouple was also used to measure the real-time focal temperature. The ultrasonic signal scattered at the focal point of HIFU irradiation was collected by the fiber hydrophone, and the attenuation coefficient was calculated. Finally, the attenuation coefficient was input into the Khokhlov-Zabolotskaya-Kuznetov (KZK) equation and combined with the Pennes equation. The thermal lesion of the porcine liver was simulated by MATLAB software.

Results: The length of the long axis of the lesion area simulated by the attenuation coefficient of cavitation was closer to the length of the long axis of the actual measured lesion area with ethanol injection, but the length of the short axis of the simulated lesion area was smaller than that of the measured lesion area. However, the length of the long axis of the lesion area simulated by the attenuation coefficient of cavitation was larger than the length of the long axis of the lesion area simulated by the attenuation coefficient of liver at room temperature. The same results were obtained for the length of short axis.

Conclusion: HIFU combined with ethanol can produce larger lesions to biological tissues and improve the therapeutic effect.

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Introduction

High intensity focused ultrasound (HIFU) focuses low-energy ultrasound in vitro on tumor lesions in vivo by using the transmission and energy deposition of ultrasound.

Through the transient high-temperature effect generated by high-energy ultrasound in the focal region, protein denaturation occurs, so as to achieve the purpose of tumor treatment [1].

The traditional treatment of tumor tissues (such as the liver tumor) is open surgery, chemotherapy, and radiotherapy. These methods have significant incidence and mortality rates, and may be related to long-term hospitalization and recovery.

However, compared with traditional methods of tumor tissues therapy, HIFU has the advantages of noninvasive, non-ionizing and fewer complications after treatment [2].

In the process of ultrasound transmission, energy attenuation will occur due to tissues absorption and acoustic scattering. The degree of attenuation will increase with the increase of transmission distance.

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At the same time, the small focal region of the HIFU transducer leads to the long HIFU treatment time, because of the mode of point superposition.

Therefore, how to improve the therapeutic effect of HIFU has become a research hotspot.

Relevant research shows that we can improve the efficiency of HIFU treatment by changing the acoustic characteristics or acoustic environment of tissues, increasing the ultrasonic energy deposition of HIFU, reducing the cavitation threshold and other mechanisms [3].

Lang et al [4] combined HIFU with absolute ethanol to treat benign thyroid nodules. They found that the combination of HIFU and ethanol was more effective than HIFU alone in the treatment of benign thyroid nodules.

Yang et al [5] found that compared with HIFU alone, HIFU combined with ethanol treatment required less treatment time and dose, which significantly reduced the pain and side effects commonly experienced by patients.

The cavitation threshold of ethanol was lower than that of water. After ethanol was injected into

biological tissues, the possibility of tissues overheating during HIFU irradiation would be reduced [6].

Cavitation means that the tiny bubbles in the medium are activated under the alternating action of positive and negative ultrasound pressure, showing a series of dynamic processes such as oscillation, growth, contraction, and collapse.

In the process of bubble collapse, there is a strong local energy release, and extreme physical phenomena such as high temperature, high pressure and jet will appear [7].

Cavitation occurs in the biological tissues due to ultrasonic pressure, and these cavitation bubbles are a complex viscoelastic medium, which can damage the surrounding biological tissues [8].

Cavitation can be divided into transient and steady-state [9,10].

Some researchers have found that cavitation plays an extremely important role in HIFU treatment, and it can significantly improve absorption of acoustic energy by tissues, resulting in the rapid increase of tissue temperature in the focal region, rupture of blood vessels, hemostasis, enhancement of cell membrane permeability and other physical phenomena [11].

Cavitation bubbles can enhance the acoustic attenuation coefficient of tissues in the focal region, and then enhance the thermal effect of ultrasound [12].

Hynynen et al. [13] have proved that when the ultrasound intensity exceeded 700 W/cm^2, cavitation occurred in the thigh muscle of dogs.

Some researchers have found that the negative pressure of the focus was related to cavitation. They thought that the necessary condition for the cavitation effect was that the negative pressure in the medium exceeded the cavitation threshold [14,15].

Bull et al. found that when a transducer with a frequency of 1.7 MHz was used to irradiate liver tissues in vitro, cavitation would occur when the negative pressure threshold exceeded 1.86 MPa [16].

Therefore, by considering the influence of ethanol on cavitation threshold, the purpose of this paper was to evaluate the influence of HIFU combined with ethanol on the lesion of porcine liver in vitro.

Materials and Methods

Experimental equipment and materials

In order to improve the treatment effect of HIFU and decrease its adverse effects, the combination of HIFU and ethanol can be used [4-6]. After slaughtering, the fresh porcine liver tissues were cut into 40 mm × 40 mm × 42 mm cubes with less blood vessels and connective tissues.

Mixing povidone and 95% ethanol in a ratio of 1:4 to remove oxygen from the water then mixed them with water in a ratio of 1:20 and poured into the water tank.

The porcine liver tissues were fixed on the sample rack and placed in the water tank directly under the HIFU transducer (PRO2008, Shenzhen, CN).

The ultrasonic transmission distance in the water was 10 cm.

Before the HIFU irradiation experiment, 0.5 ml 95% ethanol was injected into the focal region with a syringe (Zhiyu, Taizhou, CN) under the guidance of B-mode ultrasound.

In the experiment, the HIFU source was a concave spherical self-focused transducer with a circular hole at the top, which enabled the B-mode ultrasound probe to pass through.

The fiber-optic hydrophone (FOPH2000, Leutenbach, DE) was used to detect the scattered ultrasonic signal in water, and the probe of the fiber-optic hydrophone was made of special plastic material.

If it is placed in the front of the HIFU transducer, the probe will be damaged and cannot work normally, so the probe of the fiber-optic hydrophone passed through the middle aperture of the transducer and the fiber-optic hydrophone was connected with the oscilloscope.

The needle hydrophone (UTC1250VH, Hangzhou, CN) was used to detect the cavitation broadband noise signal, and which was connected with an oscilloscope (Tektronix MDO3032, Beaverton, USA). Then the detected signal was sent to computer for further processing and programming with Matlab software (R2018b, MA, USA).

The needle of thermocouple (DT-3891G, Shenzhen, CN) was placed in the focal region of porcine liver tissues during HIFU irradiation and the temperature was measured in real-time.

The acoustic rubber (QSIC018, Chongqing, CN) was placed at the bottom of the water tank to absorb the ultrasonic wave, and the position of the transducer can be moved by the computer-controlled three-dimensional mobile platform.

Calibration of HIFU output ultrasound power was performed by radiation force balance method before experiment [17].

The pressure of HIFU source was calibrated by using a calibrated membrane hydrophone (#0200, Dorchester, UK).

The liver tissues were moved into the focus of HIFU by three-dimensional mobile platform combined with B-mode ultrasound, and HIFU with a power of 5.0 W was turned on to monitor the peak temperature rise of liver.

Once the HIFU focus was detected, the position of the liver should ensure that the needle of thermocouple probe was about 3 mm away from the focus to reduce the heating artifacts caused by the thermocouple [18].

The experimental equipment for cavitation detection was shown in Figure 1.

The center frequency of the self-focused transducer, the geometric focal length, the aperture, and the diameter of the circular aperture were 1.39 MHz, 13 cm, 11 cm, and 4.7 cm, respectively.

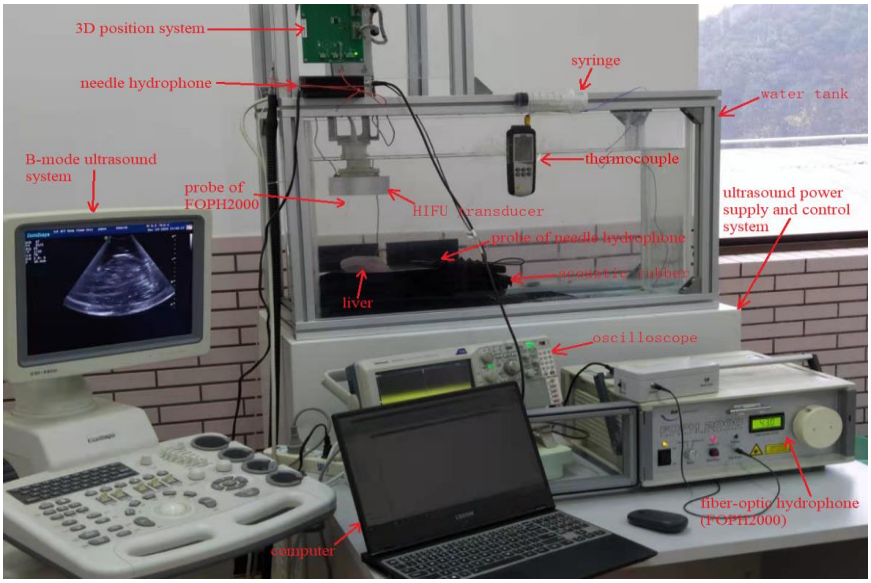


Figure 1. Experimental equipment for cavitation detection

Table 1. Acoustic and thermal parameters of water and porcine liver at room temperature

Material	ρ(kg/m^3)	c(m/s)	α(Np/cm)	B/A	C(J/kg/K)	K(W/m/K)
liver	1036	1590	8.12	6.6	3604	0.53
water	1000	1500	0.025	5.0	4180	0.60

The porcine liver tissues were continuously irradiated by HIFU transducer with 125 W and 150 W for 8 s each time, respectively.

Principle and method

In order to obtain the internal ultrasound pressure of porcine liver tissues, which were irradiated by HIFU, the Khokhlov-Zabolotskaya-Kuznetov (KZK) equation was used to simulate the ultrasound field.

The acoustic and thermal parameters of water and porcine liver tissues for simulation at room temperature (25 ℃) can be found in Table 1 [19,20].

Due to the high acoustic power of HIFU used in the experiment, cavitation was likely to occur in the process of actual irradiation for porcine liver tissues.

The detection of cavitation and the calculation of attenuation coefficient in the porcine liver will be introduced in the following section.

The occurrence of cavitation was related to the ultrasound intensity and peak negative pressure in the medium. KZK equation was used to simulate the ultrasound intensity and peak negative pressure in porcine liver tissues. The occurrence of cavitation was analyzed theoretically. KZK equation can be expressed as [21,22].

$$\frac{\partial}{\partial\tau}[\frac{\partial p}{\partial z}-\frac{\beta}{\rho c^3}p\frac{\partial p}{\partial\tau}-L_{abs}(p)]=\frac{c}{2}\Delta_{\perp}p \qquad (1)$$

Where p is the ultrasound pressure, $\tau=t-z/c$ is the delay time, $\beta=1+\frac{B}{2A}$ is the non-linear coefficient of the tissues, ρ is the tissues density, c is the ultrasound speed, $\Delta_{\perp}$ is the Laplace operator of abscissa r, $\Delta_{\perp}=\partial^2/\partial x^2+\partial^2/\partial y^2$ is expressed in the rectangular coordinate system, but $\Delta_{\perp}=\frac{1}{\mathrm{r}}\frac{\partial}{\partial r}(r\frac{\partial}{\partial r})+\frac{1}{r^2}\frac{\partial^2}{\partial\theta^2}$ is expressed in the polar coordinate system. L_{abs} is the linear operator of medium absorption and dispersion [22]

$$L_{abs}=\frac{b}{2\rho c^3}\frac{\partial^2 p}{\partial\tau^2} \qquad (2)$$

Where b is the dissipation parameter, and here b for tissue is 0.002 [23,24]. α is the absorption coefficient at a frequency f, and α_0 is the absorption coefficient at the selected frequency f_0, and $\delta=\frac{2c\alpha}{\omega^2}$ is the ultrasound diffusion rate of the biological tissues. The relationship between ultrasound attenuation coefficient α and frequency f is as follow [25,26]

$$\alpha(f)=\alpha_0(f/f_0)^{\mu} \qquad (3)$$

μ is the attenuation index, here μ for liver and water are 1.1 and 2 [27], respectively. In the frequency domain, the ultrasound pressure is expressed by Fourier series expansion as follow [28]

$$p = \sum_{n=-\infty}^{\infty} C_n \exp(jn2\pi f \tau) \tag{4}$$

Where C_n is the complex coefficient of the n th harmonic. The finite difference algorithm based on the second-order diagonal implicit Runge-Kutta method and Crank- Nicolson finite difference method were used to solve the ultrasound field [27].

The intensity at the focus of transducer can be expressed by the amplitude value of each harmonic of ultrasound pressure as below equation [29]

$$I = \frac{2}{\rho c} \sum_{n=1}^{\infty} | C_n |^2 \tag{5}$$

Biological heat transfer equation (BHTE) was also known as Pennes equation, which was used to simulate the heating and lesion formation process of HIFU [30]

$$\rho C_t \frac{\partial T}{\partial t} = \nabla . k_t \nabla T + C_b W_b (T - T_a) + Q_v \tag{6}$$

where ρ is the density of the tissue, C_t is the specific heat of the tissue, T is the temperature at time t, k_t is the thermal conductivity, C_b is the specific heat of the blood, W_b is the blood perfusion rate, T_a is the temperature at large distances, which corresponds to the initial condition value. Q_v is the heat accumulation caused by the ultrasound field, which can be expressed as

$$Q_v = 2\alpha I \tag{7}$$

The finite difference time domain (FDTD) algorithm is used to solve BHTE.

The thermal dose, an equivalent exposure time at 43 ℃ ($TD_{43℃}$), which is used to describe the thermal lesion result in equation (8), and it is calculated by the empirical method proposed by Sapareto and Dewey, it can be expressed as [30]

$$TD_{43℃} = \int_0^t R^{43-T(t)} dt \tag{8}$$

In above formula, t is the treatment time, and

$$R = \begin{cases} 0.5 & T(t) \geq 43℃ \\ 0.25 & T(t) < 43℃ \end{cases} \tag{9}$$

The formation of the lesion area requires an equivalent thermal dose of 240 minutes at 43 ℃ is equivalent to what is achieved by heating to 56 ℃ for 1.76 s [27]. The lesion area of biological tissues is related to the thermal dose. The temperature $T(t)$ of biological tissues is calculated by Pennes equation (6), then $T(t)$ is input into equation (8) and the calculated thermal dose can be obtained by equation (8).

Finally, the lesion area can be determined by the ratio of calculated thermal dose to equivalent thermal dose of 240 minutes at 43 ℃ [30,31].

Cavitation detection

Since the 1990s, more and more evidences showed that the occurrence of cavitation was considered to be the cause of strong echo area in B-mode ultrasound images.

The acoustic cavitation caused by HIFU can be monitored in real time by the formation of highlighted area in B-mode ultrasound image during HIFU treatment. Hynynen pointed out that in the experiment of HIFU in vivo to ablate the leg muscle of dog, after the first ultrasonic pulse was sent out, the inertial cavitation signal can be detected at the same time when the B-mode ultrasound highlight area appeared [13].

Vaezy et al. claimed that during the real-time ultrasound imaging observation, bright spots (believed to be cavitation bubbles) were found to escape into the vascular system of liver tissues in vivo from the focal region of transducer [32].

Therefore, it is possible to determine whether cavitation occurs when HIFU transducer irradiates porcine liver tissues by observing the strong echo area of B-mode ultrasound image.

In addition, when the peak value of the measured broadband noise signal exceeds $\sqrt{5}$ times of the peak value of the background noise, it can be considered that cavitation occurs, which is the "Rose criteria".

It ensures that the peak value of the measured broadband noise signal can be distinguished from the change of background noise with a confidence of 98% [33].

Calculation of attenuation coefficient of cavitation in porcine liver

The corresponding attenuation coefficient of cavitation in the porcine liver can be calculated according to following equation [34]

$$\alpha_t = [\ln(A_w / A_t) + \alpha_w d_t] / d_t \tag{10}$$

A_w was the beam amplitude measured by the fiber-optic hydrophone when the porcine liver was not in the irradiation path (w/o liver), A_t was the beam amplitude measured by the fiber-optic hydrophone when the porcine liver was in the irradiation path (w/ liver), and d_t was the thickness of the porcine liver.

Results

The peak negative pressure and ultrasound intensity under 125 W and 150 W HIFU irradiation can be obtained by simulation with KZK equation, as shown in Figure 2.

The value of maximum ultrasound intensity (I_m) and peak negative pressure (P_-) at the focus were shown in Table 2.

In Table 2, when the irradiation power of HIFU was 125 W, the maximum ultrasound intensity at the focal point was 3210 W/cm^2, which exceeded the ultrasound intensity of cavitation in tissue. The maximum negative pressure at the focal point was 6.6 MPa, which was higher than the cavitation threshold of liver, it meant that cavitation would occur at the focus of liver.

Under 125 W and 150 W HIFU irradiation, the thermocouple was used to measure the focus temperature change of the liver in real time under the conditions of ethanol injection (w/ ethanol) and without ethanol injection (w/o ethanol), as shown in figure 3, the temperature results were the average of five trials.

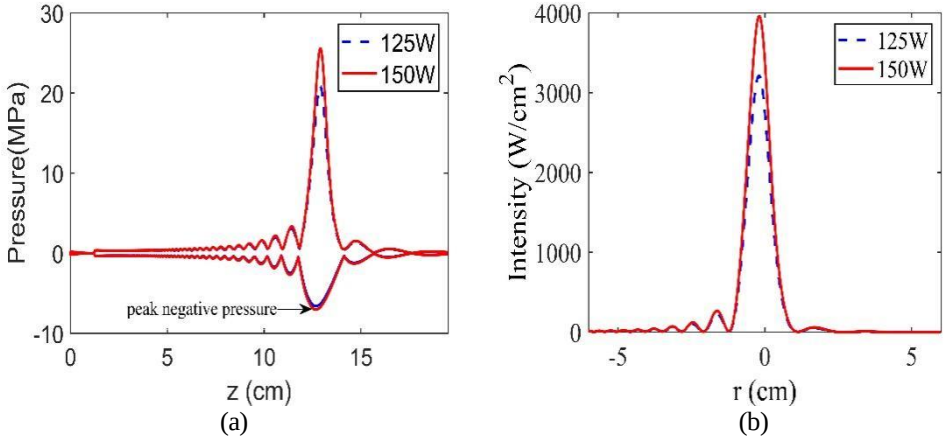


Figure 2. Simulation results of ultrasound field (a) Peak negative pressure; (b) ultrasound intensity

Table 2. Maximum ultrasound intensity and peak negative pressure under HIFU irradiation

P (W)	I_m(W/cm^2)	P_-(MPa)
125	3210	6.6
150	3957	7.0

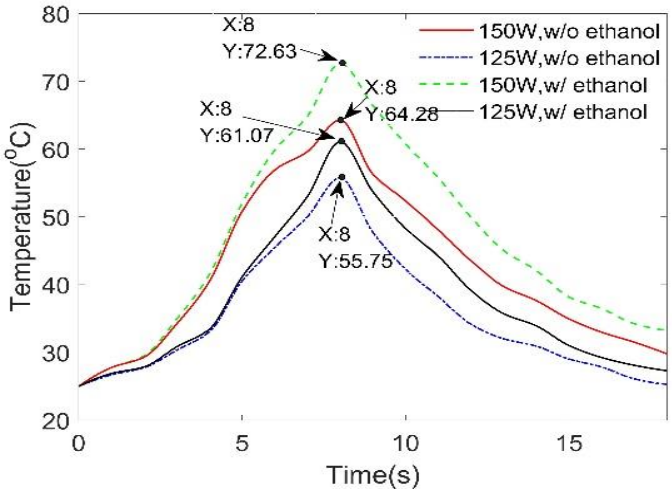


Figure 3. Measurement of focal temperature of liver irradiated by 125 W and 150 W irradiation, respectively

The liver tissues were continuously irradiated by HIFU for 8s, and then cooled down naturally.

It can be seen from Figure 3 that when the HIFU irradiation power was 125 W and 150 W, the measured maximum temperature of focus was 61.07 ℃ and 72.63 ℃ after ethanol was injected into the liver, respectively.

When HIFU irradiation power was 125 W and 150 W, but ethanol was not injected into porcine liver, the measured maximum temperature of focus was 55.75 ℃ and 64.28 ℃, respectively.

Obviously, under the same HIFU irradiation power and time, the maximum focal temperature corresponding to the

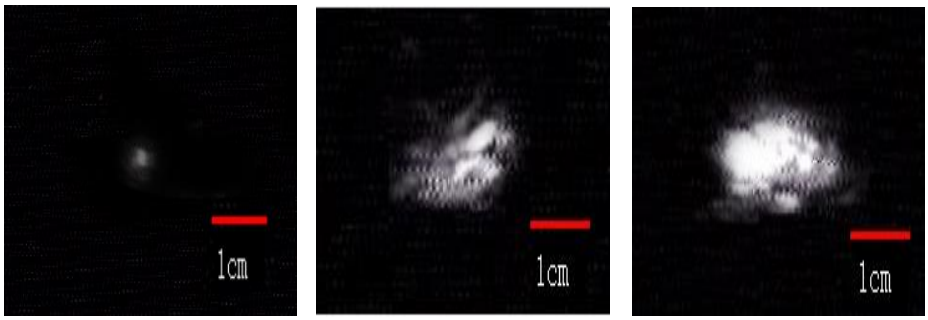
injection of ethanol into liver was higher than that corresponding to the non-injection of ethanol.

Under the guidance of B-mode ultrasound, 0.5 ml 95% ethanol was injected into the focal region of liver, and HIFU transducer was used to irradiate porcine liver tissues with 125 W and 150 W power, respectively.

It can be seen from Figure 4(a) that there was almost no strong echo area after ethanol injection but before irradiation. However, from Figure 4(b) and (c), after injection of ethanol into porcine liver tissues, the strong echo area can be observed in the B-mode ultrasound image under HIFU irradiation, indicating that cavitation occurred when HIFU transducer irradiated porcine liver tissues.

Figure 5 showed the noise signal and the background noise measured by hydrophone, when the HIFU irradiation power was 125 W. According to the "Rose criteria", the peak value of the measured broadband noise signal has exceeded $\sqrt{5}$ times of the peak value of the background noise, so cavitation would occur in porcine liver tissues under this power of irradiation.

Table 3 showed that under 125 W and 150 W HIFU irradiation, respectively, the scattered beam amplitude of ultrasound when the porcine liver was not in the irradiation path and the scattered beam amplitude of ultrasound when the porcine liver was in the irradiation path were measured, respectively, and the corresponding attenuation coefficient of the porcine liver when cavitation occurred can be calculated according to equation (10).



(a) (b) (c)

Figure 4. Three images of B-mode ultrasound captured for porcine liver:(a) after ethanol injection but before irradiation; (b) hyperecho under 125 W irradiation; (c) hyperecho under 150 W irradiation

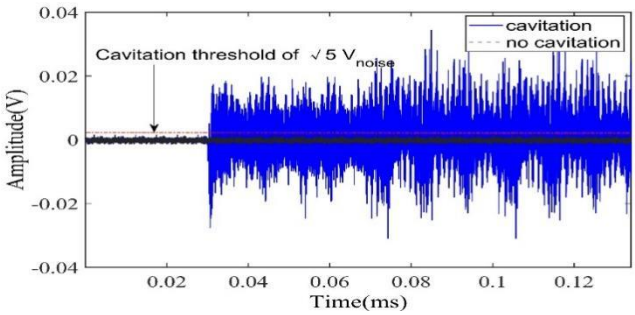


Figure 5. Detection of cavitation by needle hydrophone

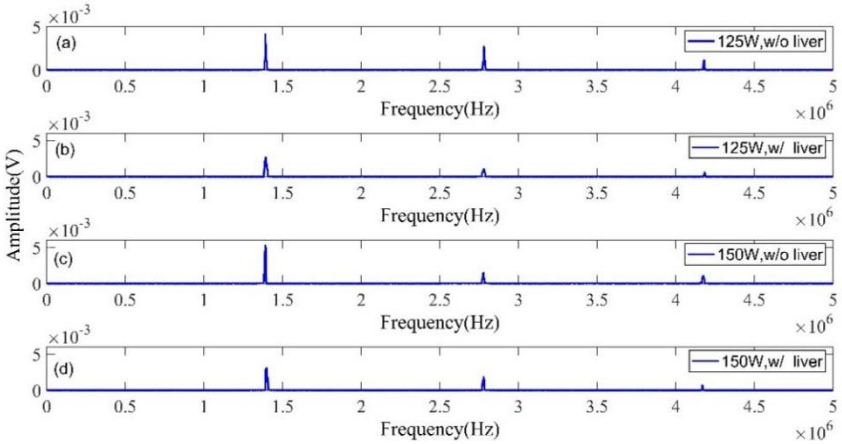


Figure 6. Amplitude spectrum for scattered signal in focal region as cavitation occurred: (a) and (c) in water without liver; (b) and (d) in water with liver

Table 3. The calculated attenuation coefficient of liver when cavitation occurred

Power(W)	Amplitude(mV)		Attenuation coefficients (Np/cm)
	A_w	A_t	
125	4.11	2.70	9.67
150	5.23	3.20	10.94

The beam amplitude corresponding to the amplitude of the fundamental wave. When cavitation occurred in the porcine liver, the measured harmonic amplitude spectrum of the scattering ultrasonic signal was shown in Figure 6.

It can be found from Table 3 that the beam amplitude and calculated attenuation coefficient under 150 W HIFU irradiation were greater than the beam amplitude and calculated attenuation coefficient under 125 W HIFU irradiation. Moreover, the attenuation coefficient calculated when cavitation occurred in the porcine liver was greater than that at room temperature (see Table 1).

The calculated attenuation coefficient when cavitation occurred in porcine liver and the attenuation coefficient in porcine liver at room temperature were input into the KZK equation for ultrasound field simulation, respectively.

The Pennes equation was established to obtain the simulated porcine liver lesion area as shown in Figure 7 (a) and Figure 8 (a). After HIFU irradiation, the liver was cut longitudinally along the middle position of the HIFU beam irradiation direction to obtain the lesion area measured as shown in Figure 7 (b), (c) and Figure 8 (b), (c).

Figure 7 and Figure 8 showed the simulated and measured lesion area for porcine liver, respectively. Both the simulated lesion area and the lesion area measured without ethanol injection were "cigar shaped", while the measured lesion area with ethanol injection was "tadpole shaped".

Table 4 showed the length of long axis and short axis corresponding to measurement and simulation under the condition of ethanol injection and without ethanol injection at the irradiation power of 125 W and 150 W, respectively.

When the irradiation power of HIFU was 125 W, it can be seen from Figure 7 (a) and Table 4, the length of long axis of simulated lesion area with and without ethanol injection was 2.11 cm and 2.01 cm, respectively.

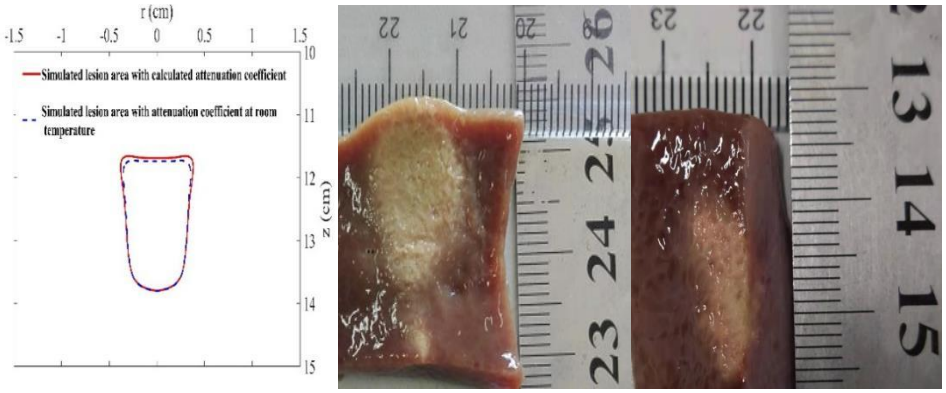
The length of short axis of simulated lesion area with and without ethanol injection was 0.76 cm and 0.68 cm, respectively.

However, the length of long axis of the measured lesion area with and without ethanol injection was 2.05 cm and 1.86 cm, respectively.

The length of short axis of measured lesion area with and without ethanol injection was 1.30 cm and 0.81 cm, respectively.

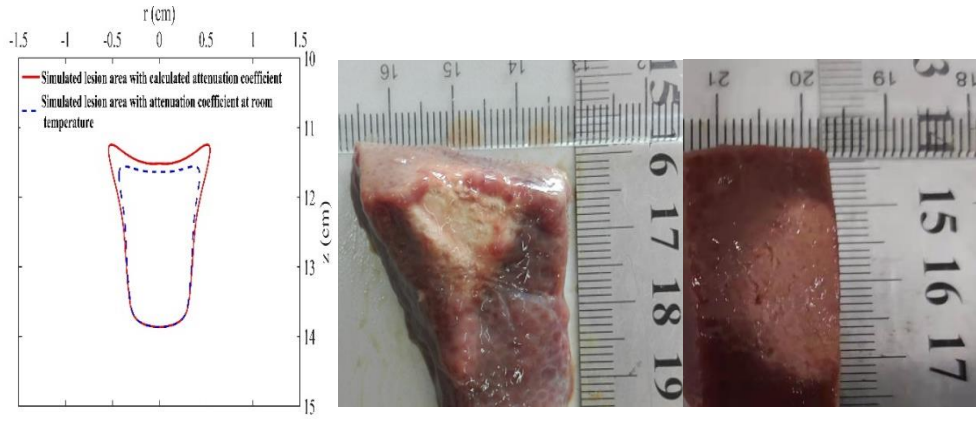
When the irradiation power of HIFU was 150 W, it can be seen from Figure 8 (a) and Table 4, the length of long axis of simulated lesion area with and without ethanol injection was 2.35 cm and 2.20 cm, respectively.

The length of short axis of simulated lesion area with and without ethanol injection was 1.06 cm and 0.86 cm, respectively. Nevertheless, the length of long axis of measured lesion area with and without ethanol injection was 2.33 cm and 2.18 cm, respectively, and the length of short axis of measured lesion area with and without ethanol injection was 1.80 cm and 1.12 cm, respectively.



(a) (b) (c)

Figure 7. Lesion area under 125 W HIFU irradiation :(a) simulation; (b)measurement with ethanol; (c) measurement without ethanol



(a) (b) (c)

Figure 8. Lesion area under 150 W HIFU irradiation:(a) simulation; (b)measurement with ethanol; (c)measurement without ethanol

Table 4. The length of long axis and short axis of lesion corresponding to simulation and measurement

Power(W)	Simulation				Measurement			
	With ethanol (cavitation)		Without ethanol (at room temperature)		With ethanol (cavitation)		Without ethanol (at room temperature)	
	long axis(cm)	short axis(cm)	long axis(cm)	short axis(cm)	long axis(cm)	short axis(cm)	long axis(cm)	short axis(cm)
125	2.11	0.76	2.01	0.68	2.05	1.30	1.86	0.81
150	2.35	1.06	2.20	0.86	2.33	1.80	2.18	1.12

Discussion

Under the HIFU irradiation power of 125 W and 150 W, the lesion induced by injecting 0.5 ml 95% ethanol into porcine liver and without ethanol injection was studied, respectively. We found that there was a strong correlation between the occurrence of cavitation and the length of long axis and short axis of the lesion in porcine liver after ethanol injection.

Compared with the attenuation coefficient of porcine liver at room temperature (see Table 1), the attenuation coefficient of porcine liver increased after ethanol injection and HIFU irradiation with different power, which was mainly caused by cavitation in porcine liver. The attenuation coefficients were 9.67 NP/cm and 10.94 NP/cm (see Table 3), respectively.

It seemed that the higher the attenuation coefficient of porcine liver, the more obvious the phenomenon of hyper echoic cavitation in porcine liver (see Fig. 4 (b) and (c)).

The attenuation coefficient was the most sensitive acoustic parameter for HIFU induced lesion, it has been shown that the lesion was associated with the increase in attenuation coefficient [35].

Under 125 W (or 150 W) HIFU irradiation condition, taking the measurement result as an example, the length of long axis (or short axis) of lesion measured after injection of ethanol into the porcine liver was longer than that measured without injection ethanol into porcine liver (see Table 4), and the simulation had a similar result.

As a result, the higher the attenuation coefficient of porcine liver, the longer the long axis (or short axis) of lesion in porcine liver.

Compared with the lesions caused by HIFU alone, it was found that the lesions in porcine liver tissues induced by ethanol combined with HIFU increased in both the length of long axis and the short axis, which indicated that ethanol moved convective in uneven liver tissue during HIFU irradiation due to acoustic flow effect.

It should be noted that the liver is a highly vascularized organ with a wide network of capillaries that allows fluid to pass between cells and tissues at a faster rate.

Therefore, HIFU combined with ethanol can significantly improve the therapeutic effect of lesion. On the other hand, ethanol has a lower boiling point than water [36,37], so ethanol injection can reduce the cavitation threshold of tissues [38], as reported in tissue-mimicking material (TMM) and bovine liver experiments [39].

The surface tension of ethanol-water mixture is less than that of water and decreases with the increase of ethanol concentration [40].

The decrease of surface tension reduces the nucleation of bubbles [41,42], and thus reduces the cavitation threshold.

Due to the complexity of cavitation, when the porcine liver was not injected with ethanol and irradiated it by HIFU, the lesion may migrate outside the targeted region, and this may be dangerous for the treatment of the targeted lesion area.

However, the injection of ethanol into the liver can prevent it from overheating beyond the boiling point of

ethanol, which can provide better control of lesions and reduce the side effects caused by cavitation [6,39].

The equivalent thermal dose standard at 43 ℃ for 240 minutes was taken as a threshold for lesion formation in the biological tissues [30]. There were some main factors affecting the lesion of porcine liver tissues under HIFU irradiation.

Firstly, the lesion caused by higher HIFU irradiation power (150 W) was greater than that of smaller HIFU irradiation power (125 W). Secondly, the lesion caused by HIFU irradiation after injecting ethanol into porcine liver was greater than that caused by HIFU irradiation alone.

Hoang et al. [6] investigated the combined effect of ethanol and HIFU on the lesion of porcine liver tissues by experiment. However, we not only investigated the combined effect of HIFU and ethanol on porcine liver lesion by experiment, but also examined cavitation with computational aspect and verified the lesion of experiment with simulation, which may be another point of view to evaluate HIFU treatment.

Conclusion

In our research work, the effect of high intensity focused ultrasound on the lesion of porcine liver tissues was studied, the cavitation threshold was reduced by injecting ethanol.

Meanwhile, the cavitation phenomenon was monitored by the needle hydrophone and B-mode ultrasound. The focal temperature of liver was measured by thermocouple in real time. The corresponding ultrasound intensity and attenuation coefficient of porcine liver tissues were calculated as cavitation occurred.

Additionally, the length of long axis and short axis differences of liver lesion induced by HIFU alone and HIFU combined with ethanol were compared.

The experimental and simulation results showed that compared with HIFU alone, HIFU combined with ethanol could cause larger lesion to porcine liver tissues, therefore, appropriate ethanol injection into biological tissues can effectively improve the therapeutic effect of HIFU.

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